SYNOPSIS

Chapter 1: Introduction to ylidenemalono/ketonitriles and their applications in organic synthesis.

Organic chemistry,[1] the branch of chemistry that deals with the study of carbon-based compounds, provides a fundamental understanding of molecular structure and reactivity. In organic chemistry, the concept of electron delocalization[2,3] refers to the distribution of electrons over multiple atoms or bonds within a molecule. This phenomenon occurs when pi (π) electrons, which are electrons in the double or triple bonds between atoms, can move freely or be shared among multiple atoms. The concept of electron delocalization is closely related to conjugation, which is the alternating pattern of single and multiple bonds in a molecule. Conjugation[4],[5] is an important aspect of organic molecules as it can significantly influence their physical and chemical properties. In a conjugated system, pi (π) electrons are able to move along a series of adjacent p-orbitals, forming a continuous network of overlapping orbitals. This delocalization of electrons stabilizes the molecule and leads to several interesting effects. This concept of electron delocalization and conjugation leads us to the push-pull system[6] where in where in one end of the molecule has an electron rich donor group and the opposite end has an electron deficient functionality. The donor "push" electrons towards the acceptor which leads to the polarization of the molecule and can influence the reactivity as well as property of the molecule. Push-pull systems are often found in organic chemistry, where molecules containing multiple bonds or polar groups can exhibit this behavior. For example, in a carbonyl group, the oxygen atom pulls electron density towards itself, while the adjacent carbon atom pushes electron density towards the oxygen atom.

Push-pull systems are equally present in inorganic and organometallic compounds, where they play a role in catalysis[7], optoelectronics,[8] conductors,[9] photovoltaics,[10] solar photon conversion[11] and other applications across various branches of modern research.

Among various push pull systems, push-pull systems of the type **1** and **2** (**Figure 1**) i.e., ylidenemalononitrile and ylideneketonitrile have been extensively studied as key intermediates or building blocks for the synthesis of various heterocyclic derivatives [12,13,14] that are having medicinal or agrochemical importance.

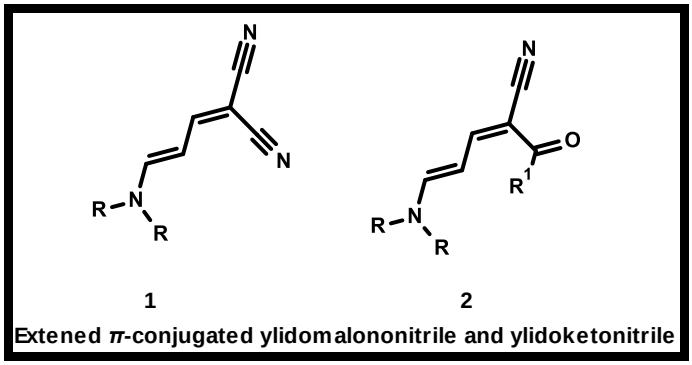


Figure 1:Ylidenemalononitrile (1) and ylideneketonitrile (2)

The enhanced utility of the ylidenemalononitrile, ylideneketonitrile push-pull systems could be seen by the number of reports from literature, a search in Scifinder^{n} (**Figure 2**) suggest that its significance is increasing progressively.

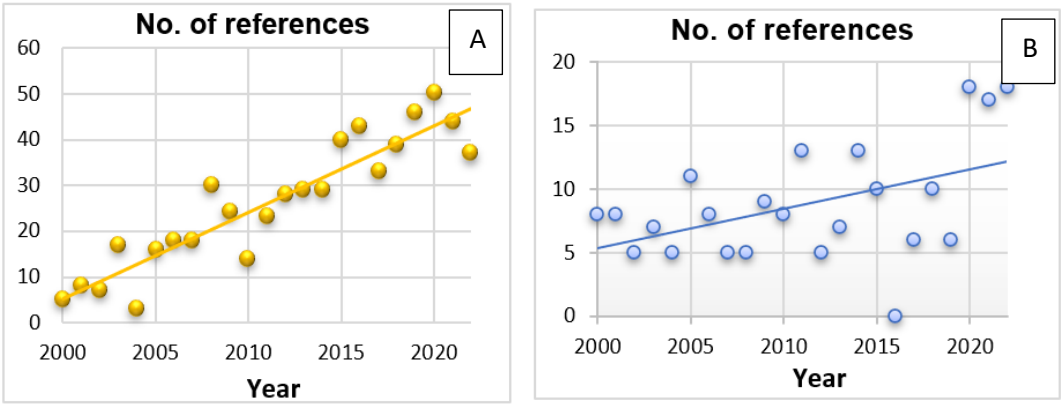


Figure 2: The usage of ylidenemalononitrile (A) / ylideneketonitriles (B) over a period 2 decades.

The presence of the electron-donating amine group and the electron-withdrawing groups like nitrile group or keto group in the molecule provides a unique reactivity that allows for the formation of a variety of heterocyclic systems, such as pyridines,[15,] pyrazoles, and pyrimidines.[16] **Figure 3** demonstrates the increased utility of these systems for the synthesis of biologically active molecules.

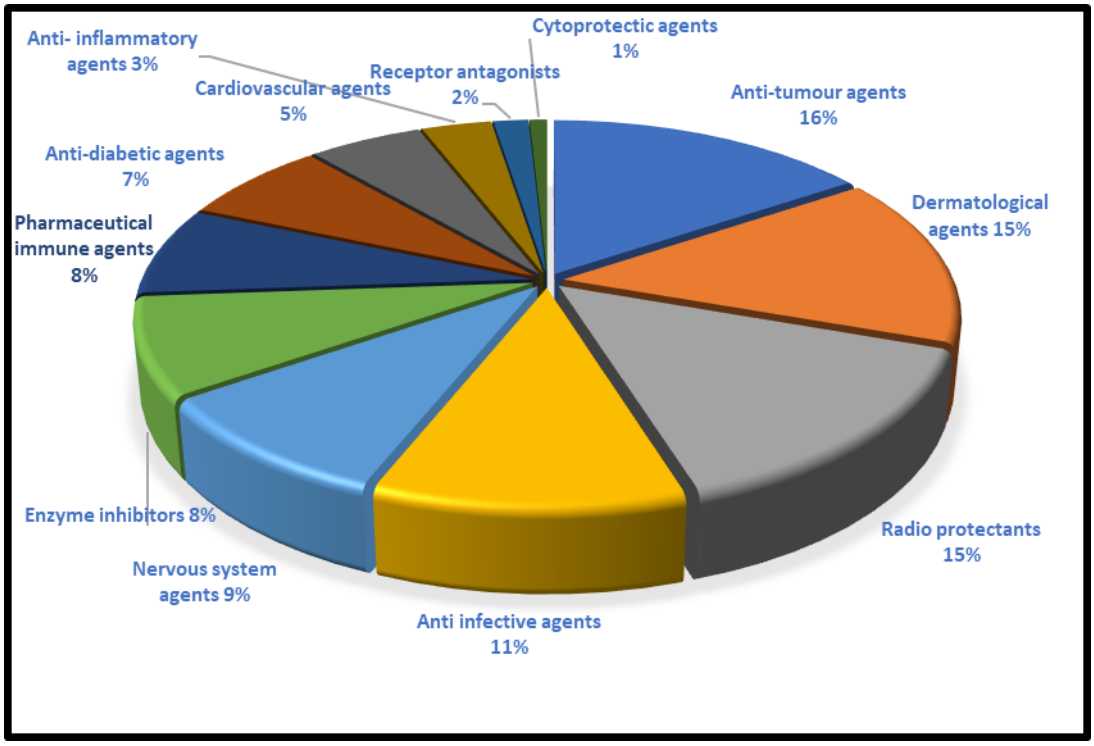


Figure 3: Biological application of ylidenemalononitrile/ylideneketonitriles

Based on the literature survey, it was evident that both the ylidenemalononitrile and ylideneketonitrile can be easily prepared using commercial raw materials in single or multiple steps and have high potential to use as building blocks for heterocycles synthesis with various applications. Most of the references showed six-membered nitrogen heterocycles are formed by reacting with ammonia under diverse reaction conditions. To our surprise, ylideneketonitrile with perfluorinated alkyl chain was not reported in literature except the trifluoromethyl ketone derivative which could be a useful building block for crop science products. Secondly, the reactions of ylideneketonitrile were reported with ammonia, but their reactivity with other amines and diamines has not been explored.

Drawing from the findings of the literature review and with a specific emphasis on the advancement of new chemical building blocks for crop protection research, we designed a hypothesis to access innovative building blocks utilizing ylideneketonitrile and a work plan was proposed to explore their reactivity, as shown in **Figure 4**.

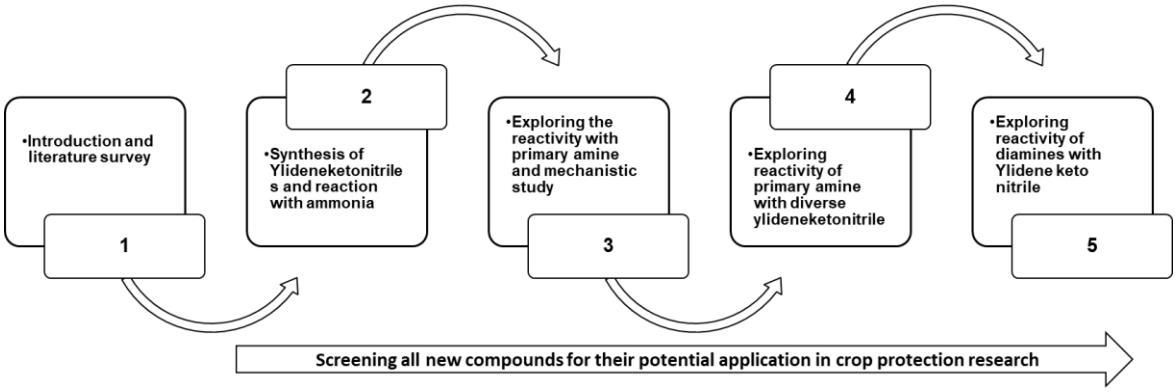

•Introduction and literature survey
1
2
•Synthesis of Ylideneketonitrile s and reaction with ammonia
•Exploring the reactivity with primary amine and mechanistic study
3
4
•Exploring reactivity of primary amine with diverse ylideneketonitrile
•Exploring reactivity of diamines with Ylidene keto nitrile
5
Screening all new compounds for their potential application in crop protection research

Figure 4: Overall thesis work plan based on the literature survey

Chapter 2: Synthesis and stability studies of various ylideneketonitriles (push-pull system) and their novel application in the synthesis of substituted pyridine derivatives.

This chapter describes the synthesis and stability studies of the push-pull systems and their application in the synthesis of substituted pyridine derivatives and their biological evaluation in agro chemistry.

Amongst various push-pull systems, ylidenemalononitriles **1** were pursued extensively as an alternative to the classical methods for accessing pyridine and various heterocyclic derivatives.[17,18,19]

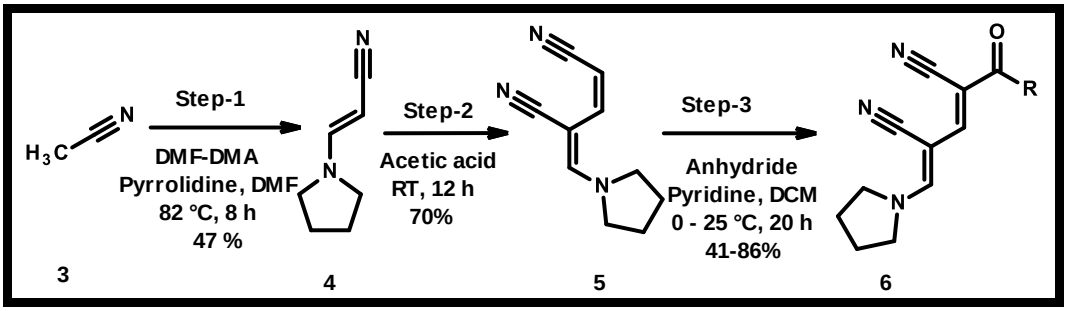
Despite the versatility of ylidenemalonotriles, the structural symmetry at the pull end of the molecule does limit their applicability in securing functional diversity on the pyridine core. As a result, we hypothesized that replacing one of the nitrile groups with a different functionality could broaden the scope of these intermediates and enable "diversity on demand" and could deliver novel pyridine derivatives.

Hence, in the current work we pursued to develop novel ylideneketonitriles and also apply the same for synthetic utility.

Synthesis of ylideneketonitriles:

Initially, we began our investigation in preparation for push-pull systems from acetonitrile **3** in 3 steps, as shown in **Scheme 1**. The first step involves condensation of acetonitrile with DMF-DMA in presence of pyrrolidine as a base in DMF at elevated temperature affording compound enamine **4** in 47% yield. In step 2, the enamine **4** was dimerized in acetic acid at room temperature to give compound **5** in 70% yield. In step 3 compound **5** was reacted

with various electrophiles in DCM and pyridine as a base to yield a push-pull system **6** with 41-86% yield without any column purification. **Note:** Compound **6f** was prepared upon reacting compound **5** with an electrophile (chloromethylene)dimethylammonium chloride in toluene as a solvent and DIPEA as a base, in 57% yield. All the products were characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, HRMS, and FTIR analysis.



Scheme 1: Synthesis of push-pull system from acetonitrile using 3-step sequence.

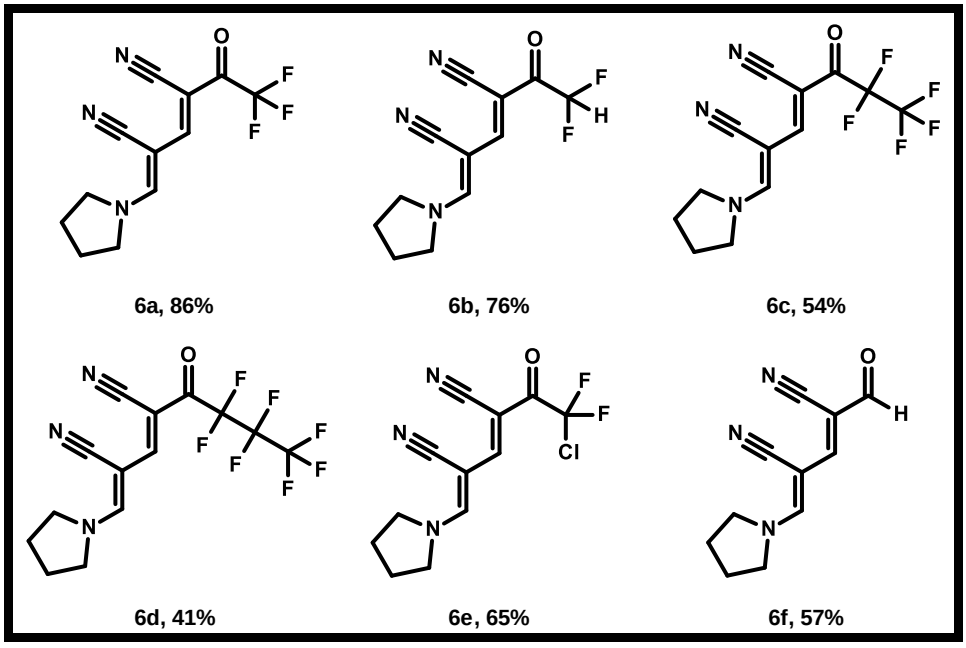
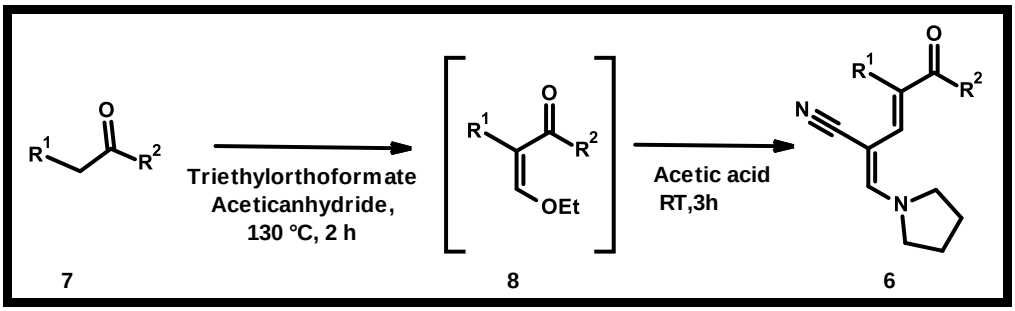


Figure 5: Diverse Push pull systems synthesised using scheme 1

During the synthesis of push pull system using intermediate **5**, we found that reactive electrophiles such as anhydrides were giving ylideneketonitriles **6,** however the strategy would limit in accessing other ylideneketonitriles. In order to circumvent this limitation, we developed a complementary approach to bring variation in R^1 and R^2 groups as shown in **Scheme 2**. In this approach, an electrophile such as ethoxymethylene(ethyl)oxonium generated upon reacting triethylorthoformate and acetic anhydride was condensed with an active methylene compound **7** to get an intermediate **8**. The intermediate **8** was then subjected to Michael addition with compound **5** in acetic acid at RT to yield a push-pull

system **6** with various substitution patterns with 43-53% yield over two steps, without any column purification. All the products were characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, HRMS, and FTIR analysis.



Scheme 2: Condensation approach to access push pull system 6

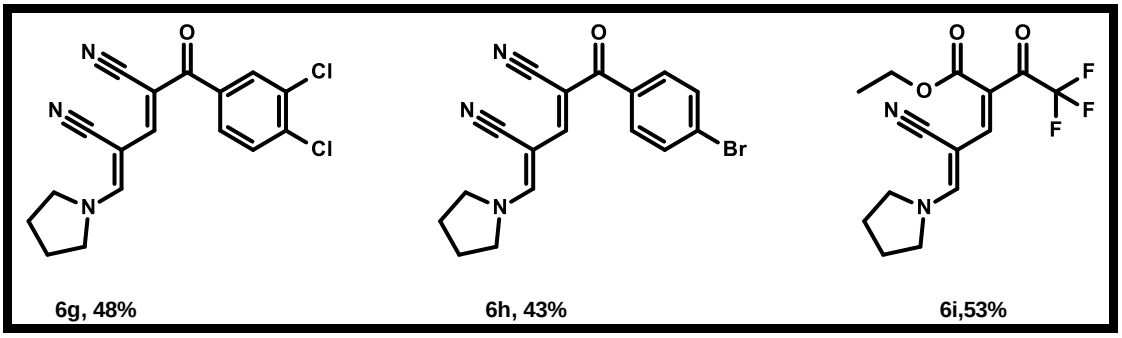


Figure 6: Push pull systems synthesized *via* condensation

Thermal stability studies of all these push-pull systems were studied using DSC,[20] as shown in **Figure 7** and **Figure 8** and following conclusion has been depicted:

1. With the exception of compound **6f**, all the synthesized push-pull systems have melting points.

2. The decomposition patterns vary among the push-pull systems. However, a consistent observation is that the starting points (left limits) for the primary exothermic process in all compounds are above 170°C

3. Among the compounds, compounds **6a** (838 J/g), **6b** (570 J/g), **6c** (499 J/g), and **6e** (664 J/g) exhibit significantly higher energy release during the first exothermic process compared to compounds **6d** (258 J/g), **6g** (191 J/g), **6h** (156 J/g), and **6i** (126 J/g). Compound **6f** shows a relatively low energy release of around 12.6 J/g during the first exothermic event, while the second exothermic event displays a higher energy release of approximately 490 J/g. In conclusion, all the synthesized push-pull systems are stable at room temperature. Although they have melting

points and exhibit diverse decomposition patterns, they remain stable under normal conditions.

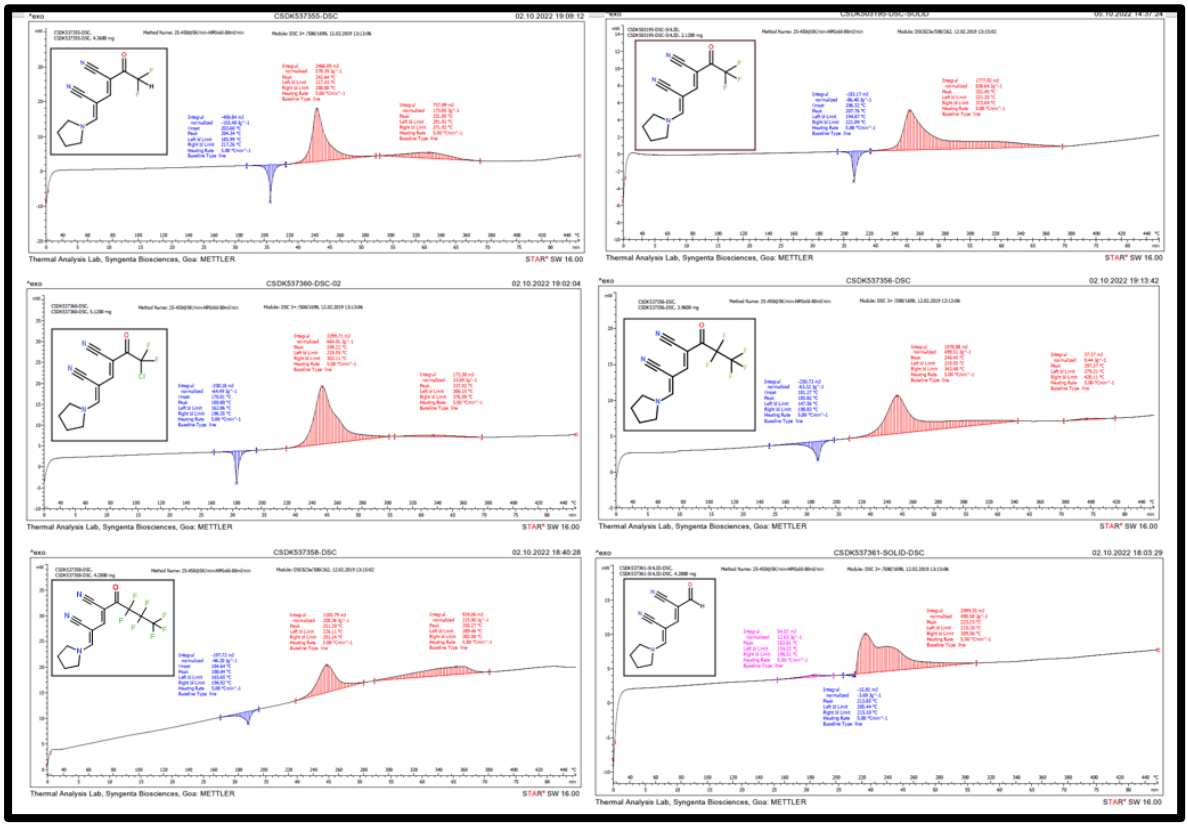


Figure 7: Thermal stability studies of push pull system by DSC.

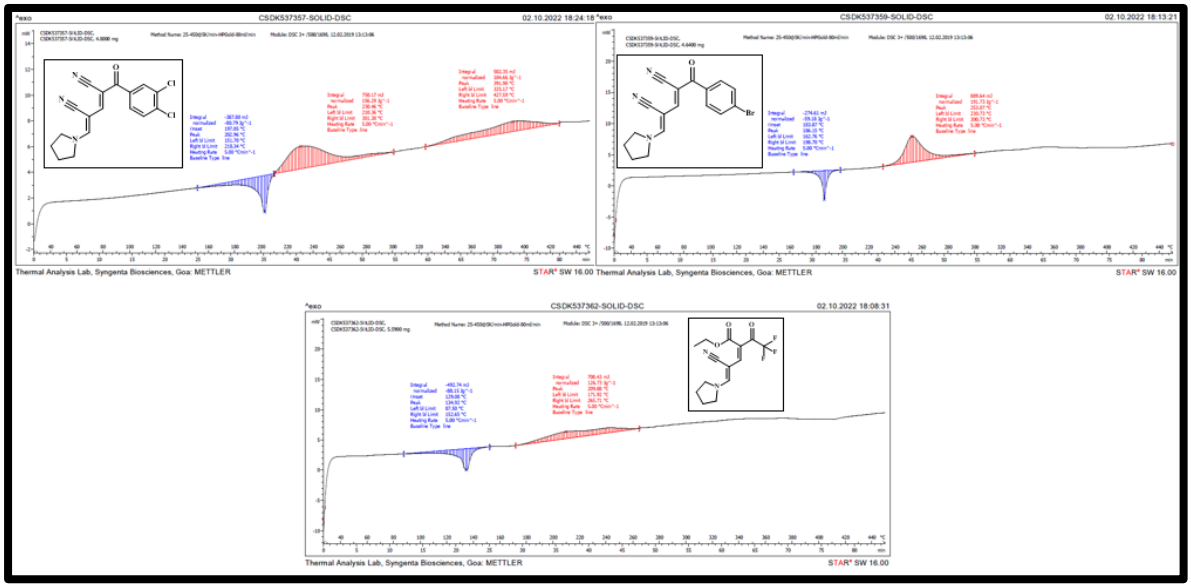
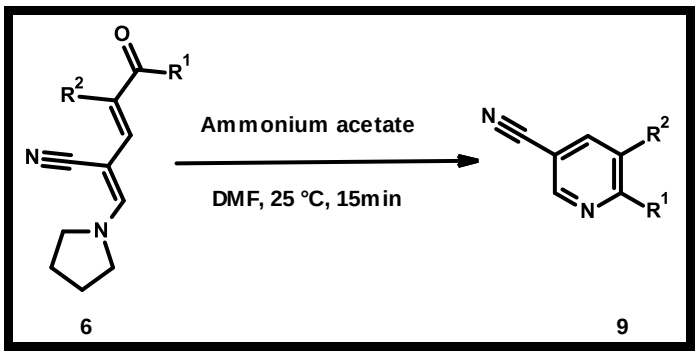


Figure 8: Thermal stability studies of push pull system by DSC.

Application of push-pull system towards the synthesis of substituted pyridine derivatives:

Ylideneketonitriles were screened for the synthesis of substituted pyridine derivative using ammonium acetate as an ammonia source. When different ylideneketonitriles **6** were treated with ammonium acetate (1.5 equiv.) in DMF solvent (10 vol.) at 25 °C (**Scheme 3**), reaction completes within 15 min to obtain substituted pyridines **9** in 79-90% yield (**Figure 9**). All the products were characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, HRMS, and FTIR analysis.



Scheme 3: Synthesis of substituted pyridine derivatives using ylideneketonitriles 6

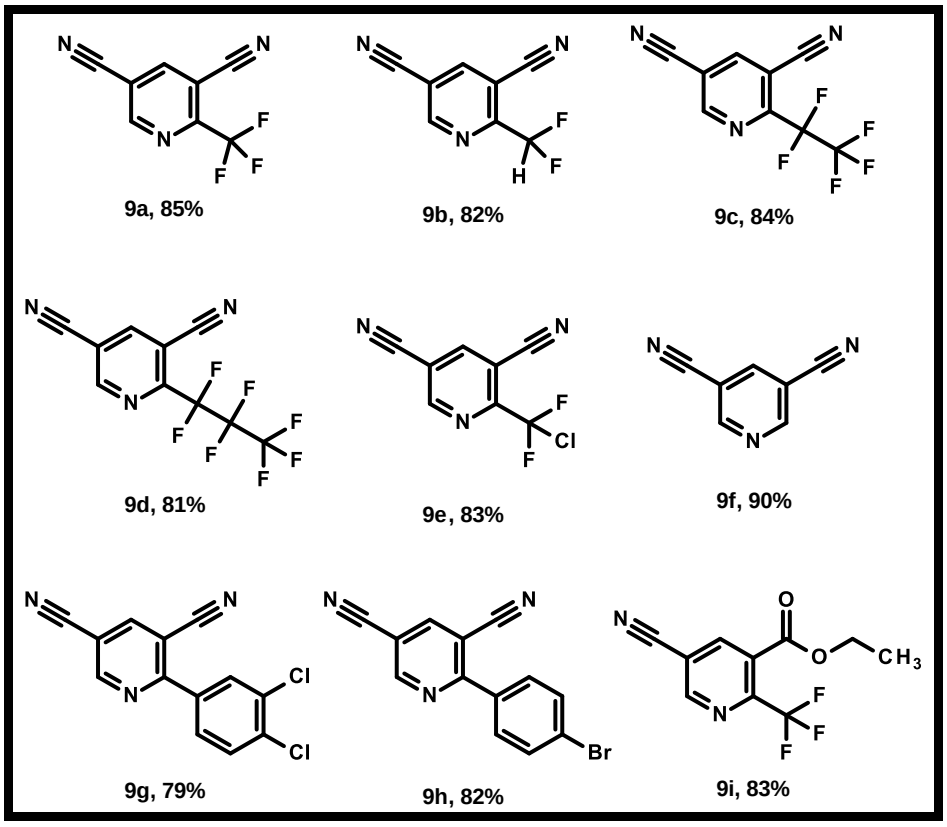


Figure 9: Substrate scope for various substituted pyridines.

Conclusion: In summary, we have synthesized nine diversely substituted ylideneketonitriles **6** utilizing simple and easily available starting materials using two different strategies. Further, these ylideneketonitriles **6** were successfully cyclized into substituted pyridine derivatives **9** under mild reaction conditions. These results demonstrate the application of push pull systems as a key building block for the synthesis of different substituted pyridine derivatives to screen for their biological applications.

Biological evaluation: All synthesized compounds were tested for their biological activity in the field of crop protection and were found to be weekly active.

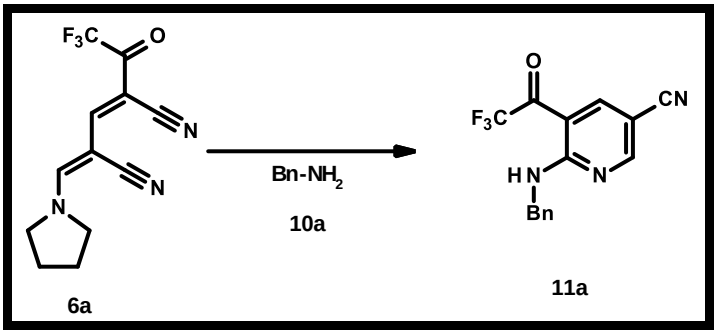
Chapter 3: Synthesis of 2-*N*-alkyl amino-3-trihaloacetyl-5-cyanopyridine derivatives and their biological evaluation

This chapter describes the utility of ylideneketonitriles towards the synthesis of 2-*N*-alkyl amino-3-trihaloacetyl-5-cyanopyridine derivatives and their potential applications in crop protection as fungicides, insecticides, and herbicides.

Introduction: The biological importance of pyridine derivatives in pharmaceutical and agro chemical research, demands new synthetic tools as an alternative to traditional methods for accessing pyridine derivatives.[21] Hence, we further extended our research for accessing highly substituted pyridine derivatives enabling “diversity on demand”. In this chapter, we extend our investigations on the reactivity of ylideneketonitriles to access 2-*N*-alkyl amino-3-trihaloacetyl-5-cyanopyridine derivatives,[22] which constitutes an important class for further functionalization. They are very good synthons for building a variety of heterocycles and drug-like molecules. Currently, there are limited methods known in the literature to access them.

Results: We started our investigation on the reactivity of ylideneketonitrile **6a** with primary amines. Firstly, ylideneketonitrile **6a** was reacted with benzylamine **10a** at 25 °C in DMF for 20 h, and to our surprise *N*-benzylpyridine-2-amine derivative **11a** yielded in 39%. The focus was shifted to the optimization of reaction conditions to get optimal yields. So, reactivity of **6a** with benzylamine was screened in various protic and aprotic solvents based on the polarity index as shown in **Table 1.** Protic solvents showed a better reaction profile with improved yield compared to aprotic solvents. The effect of temperature on the reaction profile was also studied. In methanol: water (9:1) solvent at 65 °C, the reaction was completed within 30 min (**Table 1**, **Entry 8**), however, the reaction at ambient temperature, 10-12 h stirring was necessary to ensure complete conversion.

Table 1 Solvent dependent studies for 2-*N*-alkyl amino-3-trifluoroacetyl-5-cyanopyridine synthesis



S. No.	Solvent	$E^{(N/T)}$	Temperature ^oC		Time (h)		Yield (%) of **11a**	
						Reflux temperature	RT	Reflux temperature
1	Toluene	0.099	RT	110	20	0.5	60	58
2	DCM	0.309	RT	-	20	-	65	-
3	1,4-Dioxane	0.164	RT	-	20	-	30	-
4	THF	0.207	RT	67	20	0.5	55	42
5	Ethyl acetate	0.228	RT	-	20	-	57	-
6	Methanol	0.762	RT	64	20	0.5	60	66
7	Trifluoroethanol	0.898	RT	-	20	-	26	-
8	**Methanol-water (9:1)**		**RT**	**65**	**20**	**0.5**	**67**	**69**
9	DMF	0.386	RT	-	20	-	39	-
10	DMSO	0.444	RT	-	20	-	26	-
11	Acetonitrile	0.460	RT	82	20	0.5	28	59
12	Water	1.000	RT	-	20	-	0	-

Keeping the optimized reaction conditions (**Table 1**, **Entry 8**) in hand, we further focused on the reactivity of ylideneketonitrile **6a** with different primary amines. We were successful to synthesize 2-aminopyridines **11a-g** by reacting respective primary amines **10a-g** with ylideneketonitrile **6a** in 61-88% yield under the standard reaction condition. Reaction of ylideneketonitrile **6a** with heterocyclic indolamine **10m** gave exceptionally high yield (90%).

Similarly, reaction with allyl amine **10h** also yielded compound **11h** in 82%. However, reaction of propargylamine **10i** with ylideneketonitrile **6a** gave compound **11i** in slightly lower yield of 51%. The reaction of primary amine attached to a secondary carbon **10j-k** gave higher yields **11j-k**, (75-78%) than simple primary amines **10n-p**. Under standard reaction conditions, reaction of ylideneketonitrile **6a** compounds with **10n-p** gave lower yields of **11n-p**, however, when the reaction was carried out at 25 °C gave **11n-p** in moderate to good yields (50-66%), which could be explained due to volatility of the respective amines. Relative non-volatile primary amines **10l**, **10q**, **10r** and **10s** gave product **11l, 11q-s** in 49-63% yield. To our surprise, reaction of ylideneketonitrile **6a** with aniline also gave corresponding *N*-phenylpyridin-2-amine derivative in 23% yield. However, reaction of ylideneketonitrile **6a** with highly hindered tert-butyl amine **10t** failed to deliver the compound **11t**, despite heating the reaction mixture for longer durations, this could be due to steric crowding around the nitrogen there by rendering it unreactive for 1,6-addition to ylideneketonitrile under the reaction conditions. 20 novel 2-aminopyridine derivatives were prepared with yield ranging from 23-90% as shown in **Figure 10**. All the products were characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, HRMS and FTIR analysis.

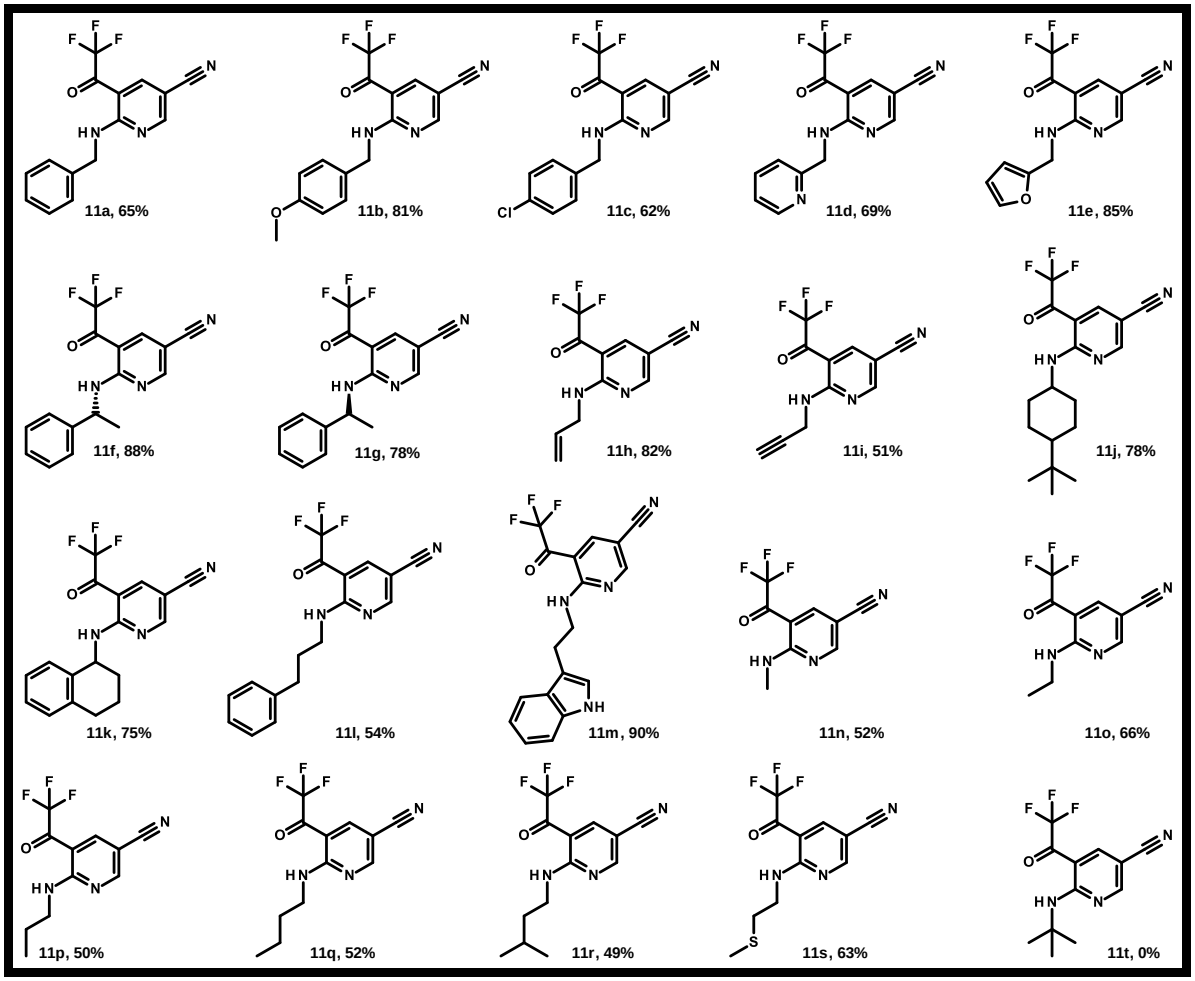


Figure 10: Substrate scope for pyridine synthesis by reaction of primary amine with 6a

Mechanistic studies:

The mechanistic investigation while complex, the trapping, isolation, and characterization of intermediate-1 and intermediate-2 unequivocally validates the product switch from intermediate-2 to *N*-alkyl-2-aminopyridine *via* Dimroth rearrangement. The key intermediates for the reaction were isolated and characterized by 2D NMR.

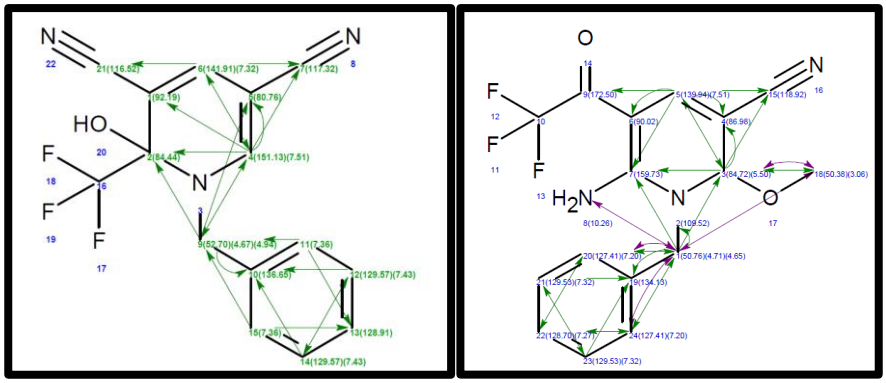


Figure 11: 2D NMR correlation of intermediate 1 and 2

In short, proposed mechanism for the formation of the product is shown in **Figure 12-A**.

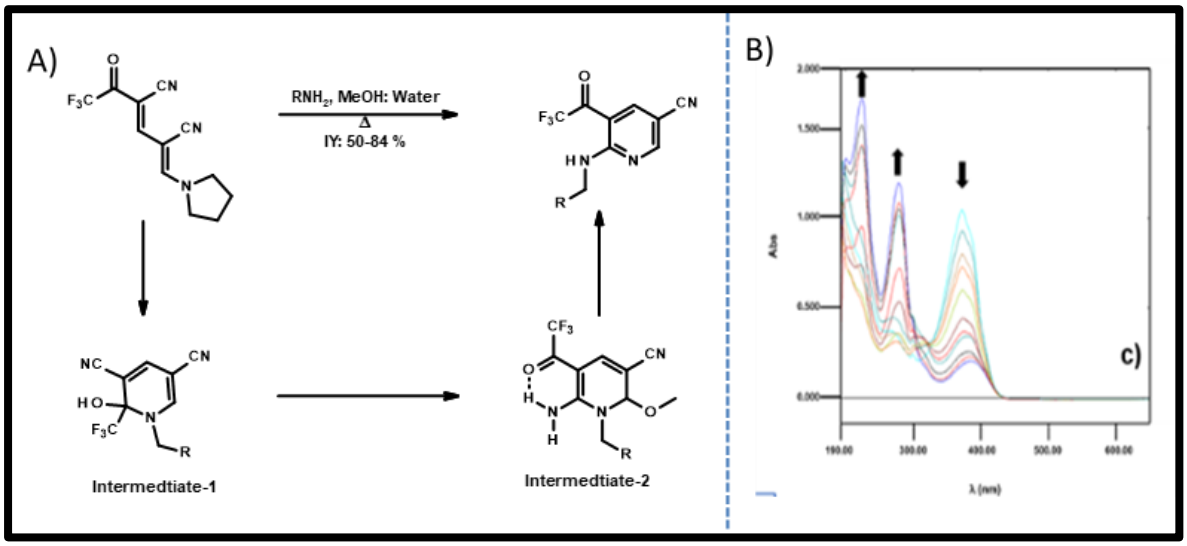


Figure 12: A) Proposed mechanism for pyridine formation from 6a via Dimroth rearrangement. B) UV-study of the reaction mass for the transformation of 6a to pyridine derivative 11a.

Compounds **6a**,**11a** and **11m** were further characterized by SC-XRD are shown below.

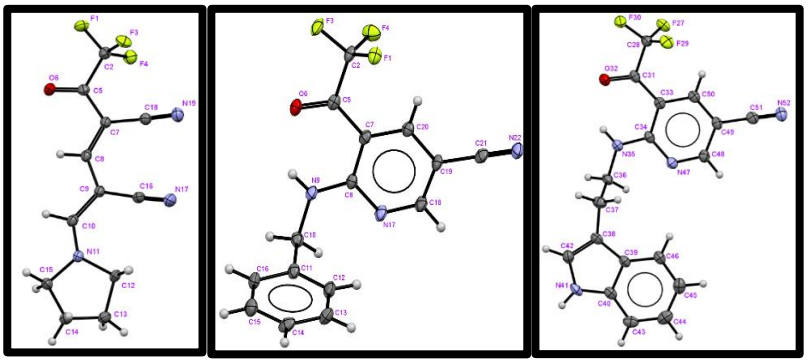


Figure 13: ORTEP representation of 6a,11a, and 11m

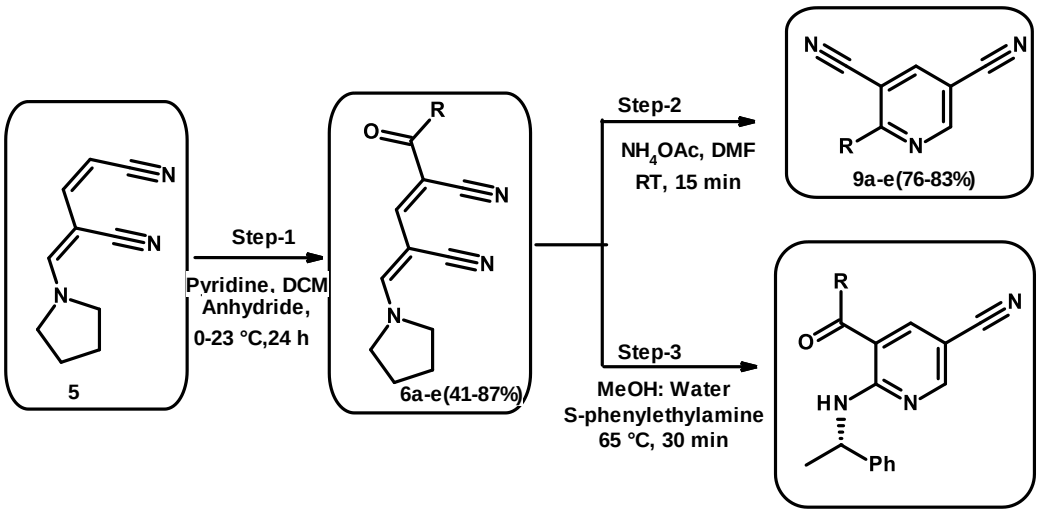
Conclusion: In conclusion, this chapter presents the reactivity of ylideneketonitrile **6a** with various primary amines resulting in the formation of novel 2-alkylamino-3,5- disubstituted pyridine derivatives **11a–s** in moderate to excellent yields (23-90%). To support the mechanism for transformation of ylideneketonitrile **6a** to 2-aminopyridines **11**, intermediate-1 and intermediate-2 were successfully isolated and fully characterized.

Biological evaluation: All synthesized compounds were tested for their biological activity in the field of crop protection and were found to be weekly active.

Chapter 4: Synthesis of 1-*N*-alkylated-3,5-dicyano-2-pyridone derivatives and 2-amino-3-chlorodifluoro acetyl-5-cyano pyridine derivatives from ylideneketonitrile and their biological evaluation.

This chapter describes the utility of ylideneketonitriles towards the synthesis of 1-*N*-alkylated-3,5-dicyano-2-pyridone derivatives and 2-amino-3-chlorodifluoro-5-cyanopyridine derivatives and their applications in agrochemistry.

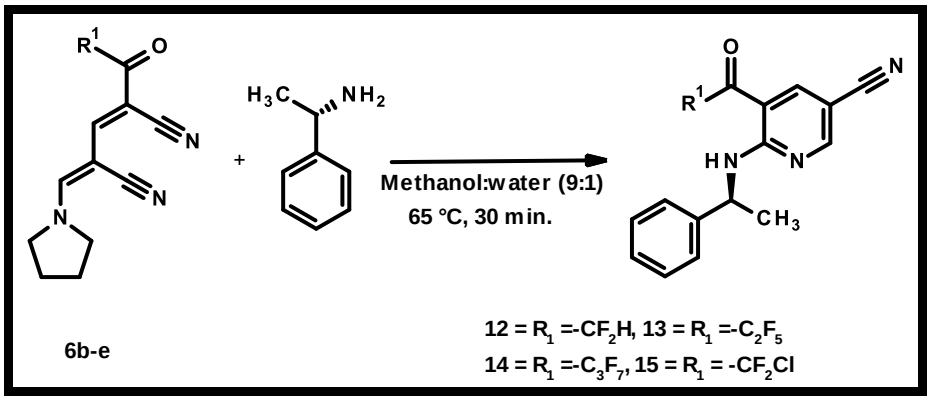
Introduction: Previously in chapter 2 and chapter 3, we have reported that Push-Pull systems **6** reacts with ammonia source to form substituted pyridines and with primary amine to form 2-amino-3-trifluoroacetyl-5-cyano pyridine derivatives. In this chapter, we were interested to study the reactivity of various push pull systems with different primary amines. Push pull system **6e** shows similar reactivity towards ammonia source but different reactivity towards primary amine in solvents with variable $E\frac{N}{T}$ values.



Scheme 4: General scheme for the synthesis of substituted pyridines and 2-*N*-alkyl amino-3-acetyl-5-cyanopyridine derivatives from push pull system.

Results:

When the reaction was carried out between (S)-(-)-1-phenylethylamine and ylideneketonitrile **6b**, **6c** and **6d** (**Scheme 5**), where the -CF_3 (**6a**) has been replaced by -CF_2H -C_2F_5, and -C_3F_7, gave the desired 2-alkylamino-3,5-disubstituted pyridines **12**, **13** and **14** in 80%, 68 % and 58% yield respectively (**Table 2**).

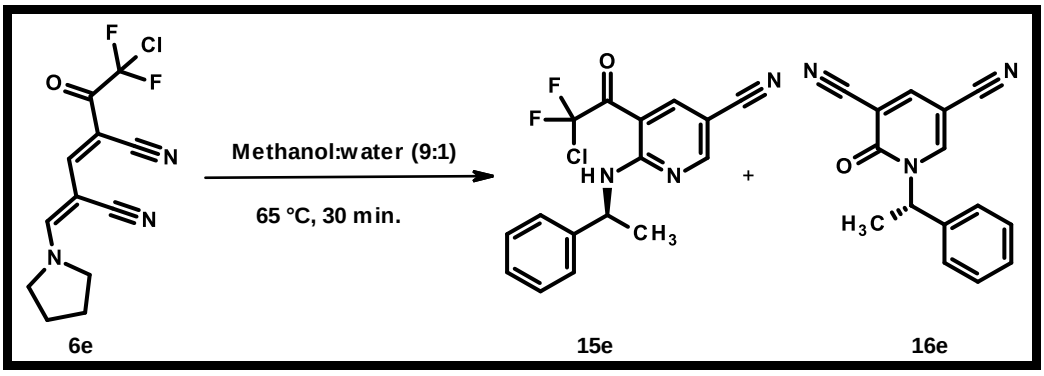


Scheme 5: Study the reactivity of 6b-e with (S)-(-)-1-phenylethylamine

Table 2: Reactivity of push pull systems 6a-e with S-(-)-phenyl ethyl amine

S.No	R_1	6 Yield (%)	Product	Yield (%)
a	-CF_3	87	11g	78
b	-CF_2H	76	12	80
c	-C_2F_5	54	13	67
d	-C_3F_7	41	14	54
e	**-CF_2Cl**	65	15e	**24**

To our surprise, when the reaction was carried out between **6e** and (S)-(-)-1-phenylethylamine, the desired product i.e. **15e** was obtained only in 24% yield along with a significant amount of 2-pyridone derivative **16e** (**Scheme 6**).



Scheme 6: Reactivity of 6e with (S)-(-)-1-phenylethylamine

Therefore, the optimization of the reaction condition was initiated with a solvent screen and hence, the model reactions were carried out between **6e** and S-(-)phenyl ethyl amine in various solvents with increasing solvent polarity parameter ($E\frac{N}{T}$). Interestingly, as the solvent polarity increased from nonpolar solvents to polar-protic a shift in product distribution was observed. To our surprise, in nonpolar solvents predominant formation of 2-pyridone **16e** was observed with trace to very poor formation of 2-alkylaminopyridine **15e** However, in presence of polar-protic solvents formation of both **16e** and **15e** was observed to varying degrees i.e. 3:1 ratio (isopropanol and methanol), 1:1 in ethanol and 6.2:1 in formamide. The unusual and erratic solvent-dependence behavior of the reaction in polar-aprotic solvent could not be rationalized with solvent properties such as *p*Ka and solvent polarity parameter. But when the reaction was carried out in trifluoroethanol, to our delight a complete switch in selectivity towards **15e** was observed.

Table 3: Solvent screening for chemo selective synthesis of 2-amino-3-chlorodifluoro-pyridine derivatives and 2-pyridone derivatives.

S.No.	Solvent	Solvent Polarity	pKa	H Bond Donor acidity	Nucleophi-licity	Pyridone 16e	Pyridine 15e
1	Toluene	0.099	43			98	2
2	1,4-Dioxane	0.164	-			100	0
3	THF	0.207	-			100	0
4	Ethyl acetate	0.228	29.5			97	3
5	Dichloromethane	0.309	-			95	5
6	DMF	0.404	35			98	2
7	DMSO	0.444	35.1			96	4
8	**Acetonitrile**	**0.460**	**31.3**			**100**	**0**
9	IPA	0.546	30.3	0.76	0.09	75	25
10	Ethanol	0.654	29.8	0.83	0.09	50	50
11	Methanol	0.762	29.0			75	25
12	Formamide	0.799	23.5			88	12
13	**Trifluoroethanol**	**0.898**	**17.9**	**1.51**	**-2.78**	**5**	**95**
14	Heptafluoro-isopropanol (HFIP)		9.3	1.96	-3.93	-	-

Using the optimised conditions, in trifluoroethanol as solvent at RT for 20-48h, 12 novel 2-amino-3-trihaloacetyl-5-cyano pyridine derivatives **15a-l** were synthesised from respective amines and ylideneketonitrile **6e** with yield ranging from 60-77% as shown in **Figure 14**.

The reactivity of ylideneketonitrile **6e** with simple aniline and aromatic amines containing electron donating groups took long duration (48 hours) for complete conversion and yielded low to moderate yields (26-58%). However, aromatic amines containing an electron withdrawing group did not result in the formation of pyridone. All the products were characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, HRMS and FTIR analysis.

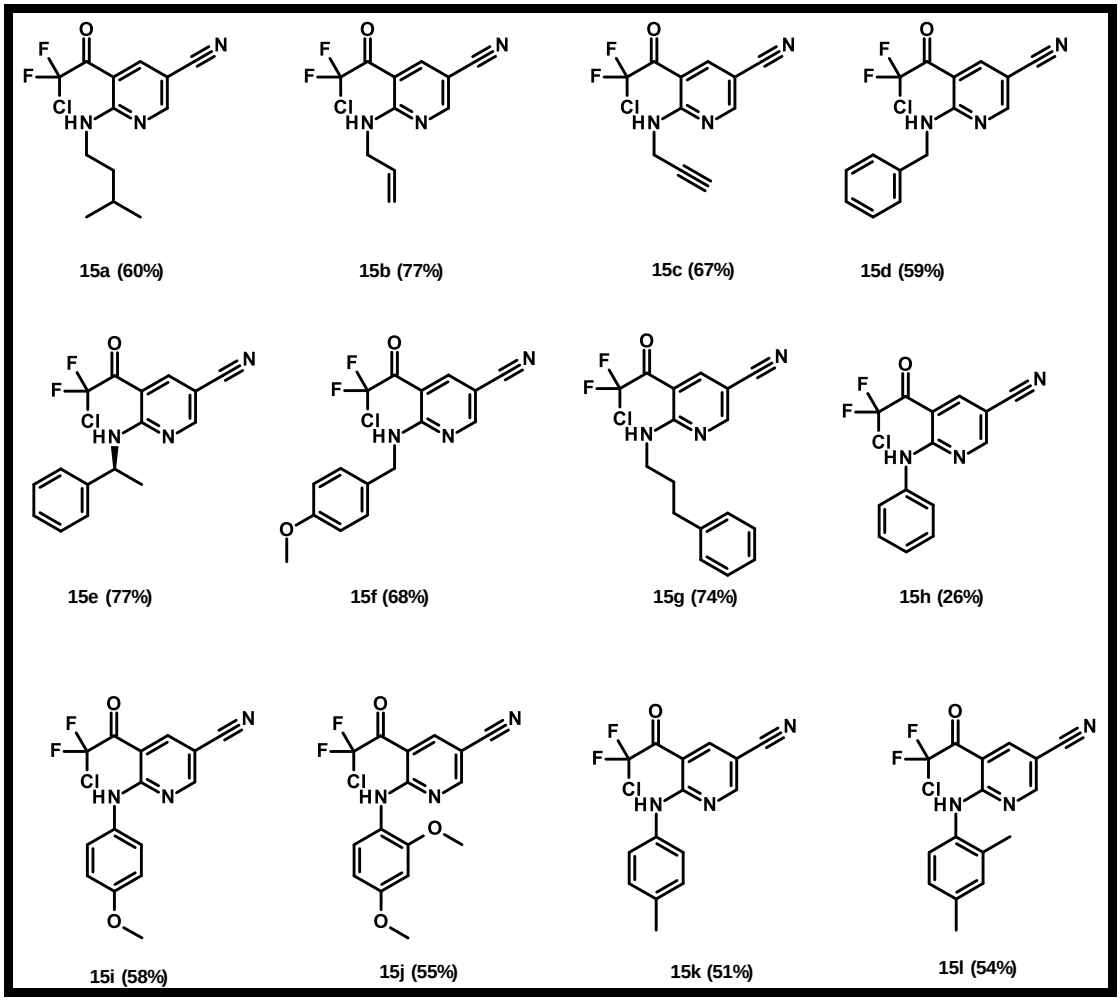


Figure 14: Synthesis of 2-amino-3-chlorodifluoro-acetyl-5-cyano pyridine derivatives using trifluoroethanol as solvent.

Similarly in acetonitrile at RT for 20 h, 13 novel 1-*N*-alkylated-3,5-dicyano-2-pyridone derivatives **16a-m** were synthesised from respective amines and ylideneketonitrile **6e** with yield ranging from 70-91% as shown in **Figure 15**. However, reactivity of Ylideneketonitrile **6e** with aromatic amines did not result in pyridone formation. All the products were characterized by ^{1}H NMR, ^{19}F NMR, ^{13}C NMR, HRMS and FTIR analysis.

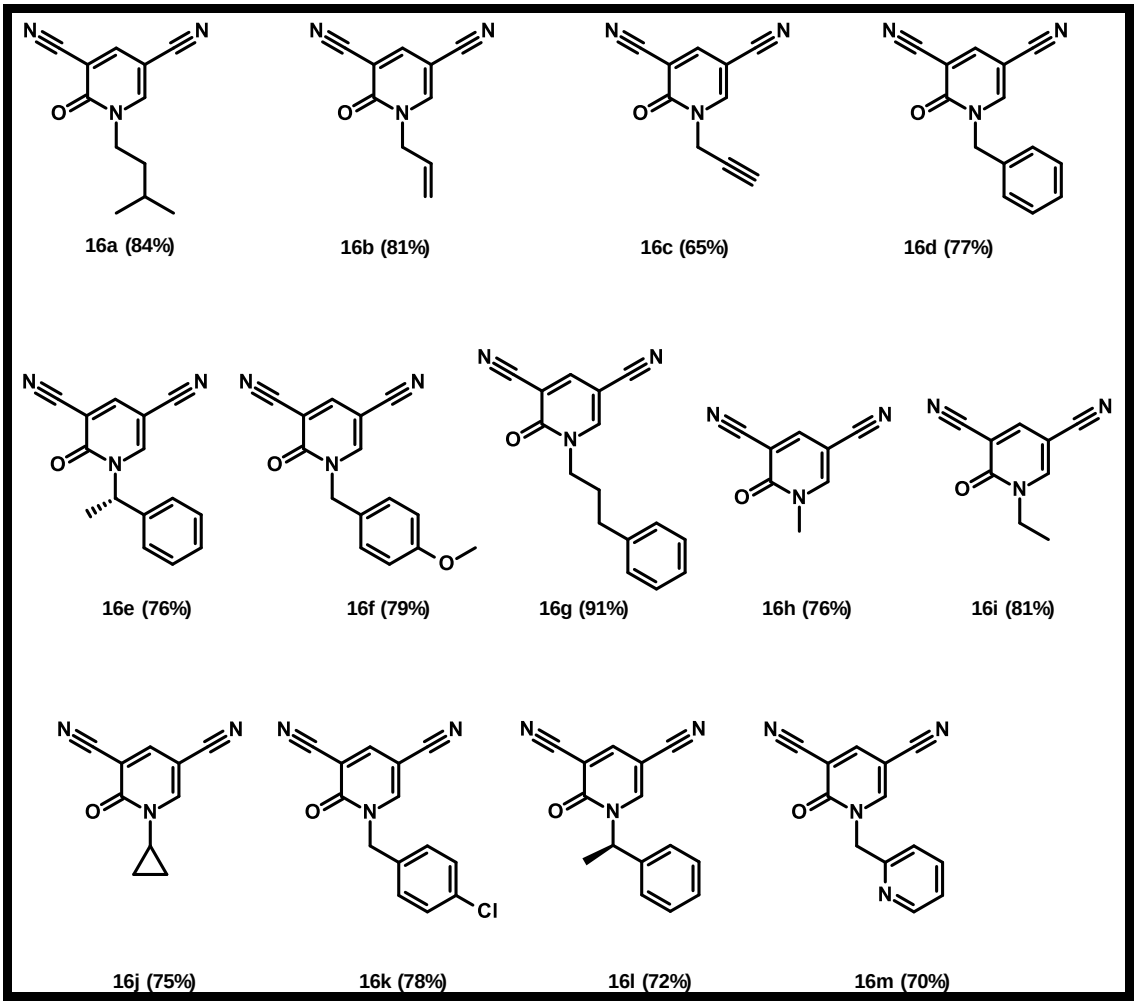


Figure 15: Synthesis of 1-N-alkylated-3,5-dicyano-2-pyridone derivatives using acetonitrile as solvent.

Mechanistic studies:

The mechanistic investigation suggests the formation of 2-*N*-alkylated-3,5-disubstituted pyridine derivative via Dimroth rearrangement and that of 1-*N*-alkylated-3,5-dicyano-2-pyridone derivative via elimination of CF_2ClH or CF_3H.

Conclusion:

This chapter presents the chemo selective and solvent dependent reactivity of ylideneketonitrile **6e** with various primary amines resulting in the formation of novel 2-*N*-alkylated-3,5-disubstituted pyridine derivative **15a-l** in moderate to good yields (26-77%) in trifluoroethanol as solvent and 1-*N*-alkylated-3,5-dicyano-2-pyridone derivative **16a-m** in good to excellent yields (70-91%) in acetonitrile as solvent. The mechanistic investigation while complex, the trapping, isolation, and characterization of a common intermediate

unequivocally validates the formation of pyridine via Dimroth rearrangement and the formation of pyridone via elimination of $-CF_2ClH$ or $-CF_3H$.

The chemoselectivity further demonstrates the synthetic utility of the methodology i.e. “diversity on demand” allowing access to various pyridine or pyridone derivatives from push-pull system.

Biological evaluation: All synthesized compounds were tested for their biological activity in the field of crop protection and were found to be weekly active.

Chapter 5: Synthesis of pyrido1,4-diazepine derivatives from ylideneketonitrile and their biological evaluation.

This chapter describes the utility of ylideneketonitriles towards the synthesis of 1,4-Diazepine derivatives and to study their applications in agrochemistry as fungicides, insecticides, and herbicides.

Introduction:

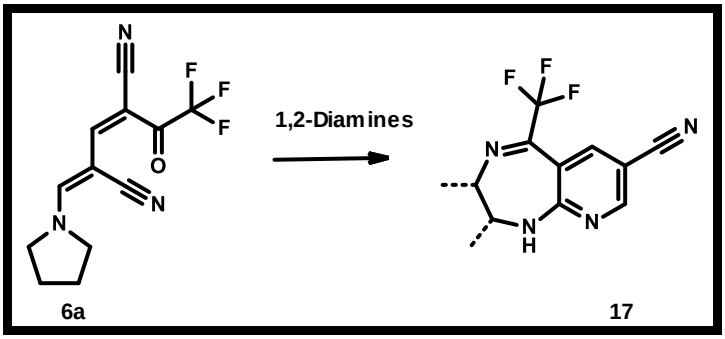
1,4-Diazepines are seven membered heterocyclic compounds containing two nitrogen heteroatoms and are associated with a wide range of biological activities. Scientists have been actively involved in the synthesis, reactions, and biological evaluation of 1,4-diazepines for decades due to their medicinal importance or biological activities like antipsychotic, anxiolytic, anthelmintic, anticonvulsant, antibacterial, antifungal and anticancer.[23] 1,4-diazepine derivatives with high biological activity could be investigated for use in the pharmaceutical industry.

The immense amount of research on benzo1,4-diazepines resulted in the synthesis of heterocycle-fused diazepine derivatives with potential pharmacological activity. Pyridoa1,4-diazepines are recognized to be active in the central nervous system and have a comparable activity to the well-known benzodiazepines. This makes the synthesis and the study of pyrido1,4-diazepines an important research topic. Despite the fact that these structures are very similar to benzo1,4-diazepines, much less work has been published on their synthesis or derivatization. As a result, there is a need to further develop these classes of unexplored scaffolds in order to discover new chemistry, methodology, and thus biological features.[24]

This chapter explores the reactivity of ylideneketonitriles (push-pull systems) towards the synthesis of such pyrido-annelated 1,4-diazepines derivatives

Results:

While accessing the reactivity of push pull system **6a** with 1,2-diamino compounds (**Scheme 7**), the formation of pyrido1,4-diazepine derivative was observed and then various pyrido1,4-diazepine derivatives **17a-j** were synthesized using different 1,2-diamino compound (**Figure 16**).



Scheme 7: General scheme for the synthesis of pyrido-1,4-diazepines.

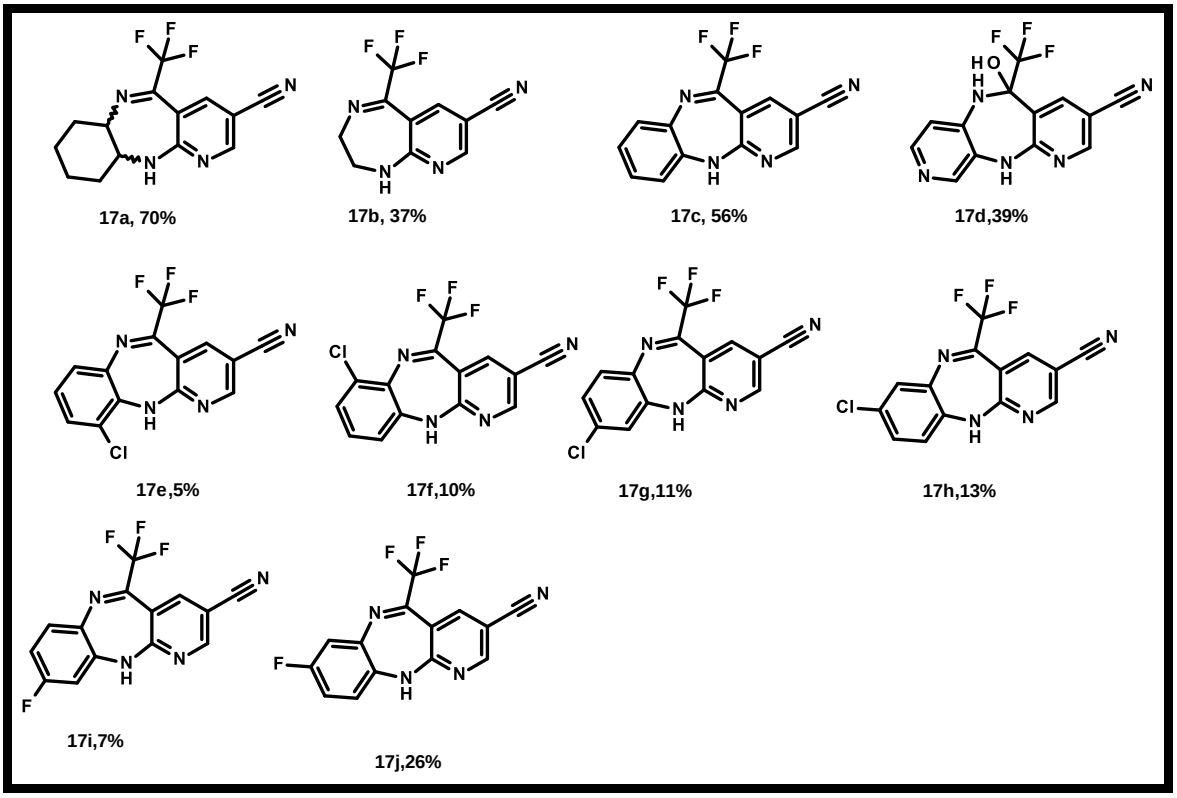


Figure 16: Pyrido1,4-diazepine derivatives synthesized from push pull system using different 1,2-diamines.

Derivatization:

The secondary amine group in **17a** was converted to amide functionality **18a-i** as shown in **Figure 17**, using various anhydrides/acids respectively, and all the molecules were tested for their biological activity in the field of crop protection.

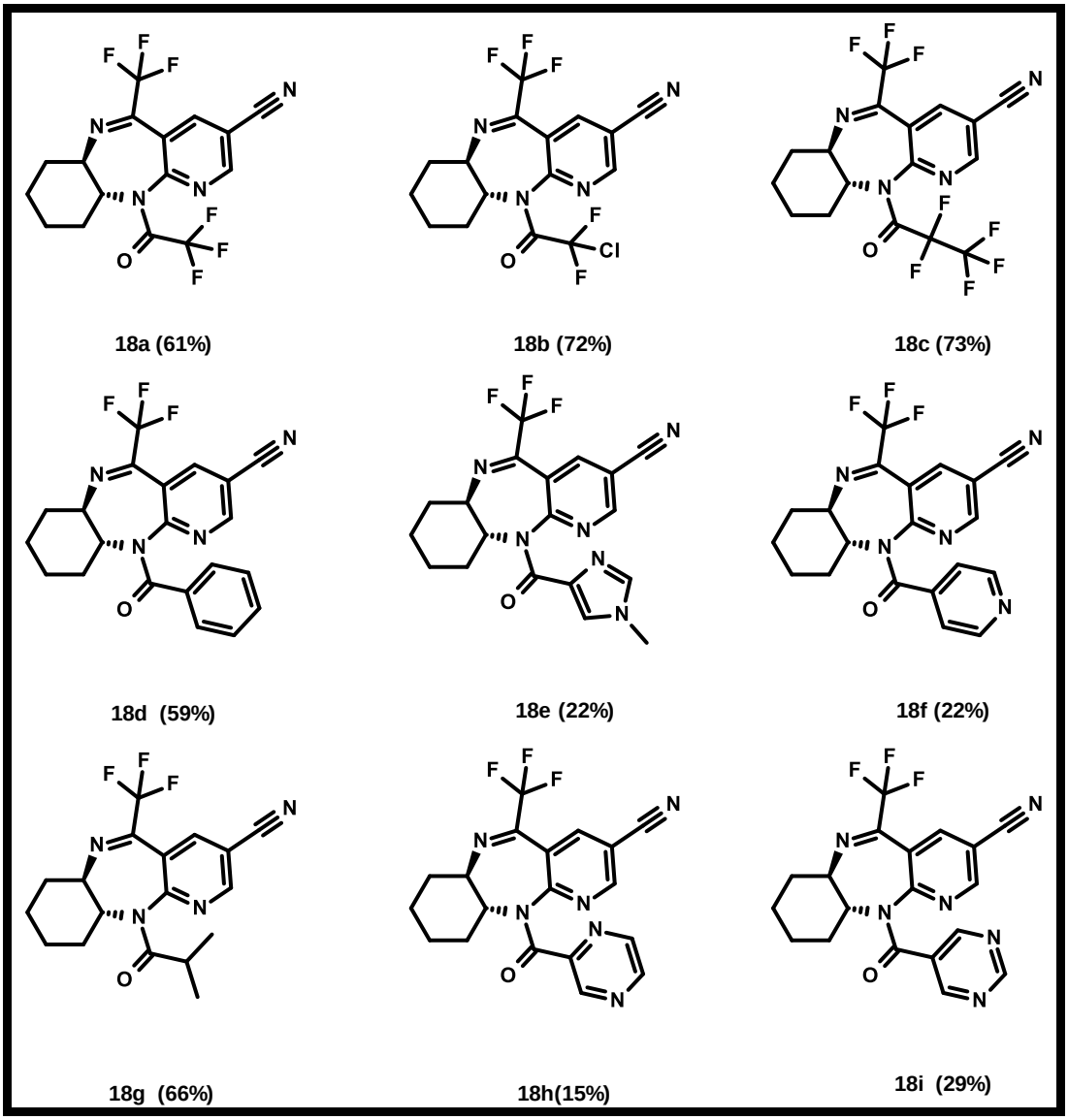


Figure 17: Compounds synthesized upon derivatization of 17a

Conclusion: This chapter presents the reactivity of ylideneketonitrile **6a** with various 1,2-diamines, resulting in the formation of novel Pyrido-annulated 1,4-diazepine derivatives (5-70%).

Biological evaluation:

All synthesized compounds were tested for their biological activity in the field of crop protection and were found to be weekly active.

References:

1 Solomons, T. G., & Fryhle, C. B. Organic chemistry. **2008**. John Wiley & Sons.

2 Liebman, J. F., & Greenberg, A. Modern models of bonding and delocalization. **1988**. VCH Publishers.

3 Herges, R., & Geuenich, D. Delocalization of electrons in molecules. J. Phys. Chem., 2001,105, 3214

4 Thiele, J. Zur Kenntniss der ungesättigten Verbindungen. Theorie der ungesättigten und aromatischen Verbindungen. Justus Liebigs Annalen der Chemie, **1899**, *306*, 87-142.

5 McNaught, A. D. Compendium of chemical terminology (Vol. 1669).**1997**, Oxford: Blackwell Science.

6 Fundamental aspects of property tuning in push–pull molecules. Bureš, F. RSC Adv., 2014, 4, 58826.

7 “Push–Pull π+/π–”(PPππ) systems in catalysis. Alegre-Requena, J.V.; Marques-Lopez, E.; Herrera, R.P. *ACS Catal.,* **2017**, *7*, 6430.

8 (*a*) Special issue on “Organic electronics and optoelectronics”, ed. Forrest, S. R.; Thompson, M. E. *Chem. Rev.*, **2007**, *107*, 923; (*b*) Special issue on “Materials for electronics”, Miller, R. D.; Chandross, E. A. *Chem. Rev.*, **2010**, *110*, 1; (*c*) Special issue on “Molecular electronics – from a visionary concept towards reality”, ed. Mayor, M. *Chimia*, **2010**, *64*, 348.

9 Special issue on “Molecular conductors”, Batail, P. *Chem. Rev.,* **2004**, *104*, 4887.

10 (a) Special issue on “Organic photovoltaics”, Bredas, J. L.; Durrant, J. R. *Acc. Chem. Res.,* **2009**, *42*, 1689; (b) Lin, Y.; Li, Y.; Zhan, X. *Chem. Soc. Rev.,* **2012**, *41*, 4245.

11 Special issue on “Solar photon conversion”, Nozik, A. J.; Miller, J. R. *Chem. Rev.,* **2010**, *110*, 6443.

12 (a) Convenient access to new 4-substituted aminopyrido [2, 3-d] pyrimidine derivatives. Belhadj, F.; Kibou, Z.; Cheikh, N.; Choukchou-Braham, N. and Villemin, D. *Tetrahedron Lett.,* **2015**, *56*, 5999. (b) Ring Closure of Ylidenemalononitriles. III. Formation of Six-Membered Rings and Related Chemistry. Campaigne, E.; Maulding, D.R. and Roelofs, W.L. *J. Org. Chem.*, **1964**, *29*, 1543. (c) Substituted butyrolactones from ylidenemalononitriles. Campaigne, E. and Ellis, R.L. *ChemComm.*, **1966**, *5*, 140.

(d) Cyclization of ylidenemalononitriles. V. Formation of substituted. gamma.-lactones. Campaigne, E. and Ellis, R.L. *J. Org. Chem*., **1967**, *32*, 2372. (e) Reaction of aldimine anions with vinamidinium chloride: Three-component access to 3-alkylpyridines and 3-alkylpyridinium salts and access to 2-alkyl glutaconaldehyde derivatives. Wypych, J. C.; Nguyen, T. M.; Benechie, M.; Marazano, C. *J. Org. Chem*. **2008**, *73*, 1169.

13 (a) New synthesis of aryl substituted 3-azapyrylium salts and their reaction with CH-acidic compounds. Schmidt, R. R. *Chem. Ber.* **1965**, *98*, 3892. (b) Synthesis of Aminonicotinonitriles and Diaminopyridines through Base-Catalyzed Ring Transformation of 2 H-Pyran-2-ones. Farhanullah, N.; Agarwal, N.; Goel, A.; Ram, V. J. J. *J. Org. Chem.,* **2003**, *68*, 2983. (c) Solventless convenient synthesis of new cyano-2-aminopyridine derivatives from enaminonitriles. Villemin, D.; Belhadj, Z.; Cheikh, N.; Choukchou-Braham, N.; Bar, N.; Lohier, J.-F. *Tetrahedron Lett*., **2013**, *54*, 1664. (d) Synthese von 4-Dimethylamino-1, 3-butadien-1, 1-dicarbonitrilen und deren Cyclisierung zu 2-Amino-3-cyanopyridinen. Ege, G.; Frey, H. O.; Schuck, Eine neue. *Synthesis*, **1979**, *5*, 376

14 Increasing Scope of Clickable Fluorophores: Electrophilic Substitution of Ylidenemalononitriles. de Souza, J.M.; Abdiaj, I.; Chen, J.; Hanson, K.; de Oliveira, K.T.; McQuade, D.T. *J. Org. Chem. Res.,* **2020** ,*85*, 11822.

15 (a) Convenient access to new 4-substituted aminopyrido [2, 3-d] pyrimidine derivatives. Belhadj, F.; Kibou, Z.; Cheikh, N.; Choukchou-Braham, N. and Villemin, D. *Tetrahedron Lett.,* **2015**, *56*, 5999. (b) Ring Closure of Ylidenemalononitriles. III. Formation of Six-Membered Rings and Related Chemistry. Campaigne, E.; Maulding, D.R. and Roelofs, W.L. *J. Org. Chem*., **1964**, *29*, 1543. (c) Substituted butyrolactones from ylidenemalononitriles. Campaigne, E. and Ellis, R.L. *ChemComm.*, **1966**, *5*, 140. (d) Cyclization of ylidenemalononitriles. V. Formation of substituted. gamma.-lactones. Campaigne, E. and Ellis, R.L. *J. Org. Chem*., **1967**, *32*, 2372. (e) Reaction of aldimine anions with vinamidinium chloride: Three-component access to 3-alkylpyridines and 3-alkylpyridinium salts and access to 2-alkyl glutaconaldehyde derivatives. Wypych, J. C.; Nguyen, T. M.; Benechie, M.; Marazano, C. *J. Org. Chem*. **2008**, *73*, 1169

16 de Souza, J. M., Abdiaj, I., Chen, J., Hanson, K., de Oliveira, K. T., & McQuade, D. T.Increasing Scope of Clickable Fluorophores: Electrophilic Substitution of Ylidenemalononitriles. *J. Org. Chem. Res.,* **2020** ,*85*, 11822

17 (*a*) Belhadj, F.; Kibou, Z.; Cheikh, N.; Choukchou-Braham, N. and Villemin, D. 2015. Convenient access to new 4-substituted aminopyrido [2, 3-d] pyrimidine derivatives. *Tetrahedron Lett.*, **2015**, *56*, 5999. (*b*) Campaigne, E.; Maulding, D.R. and Roelofs, W.L. Ring Closure of Ylidenemalononitriles. III. Formation of Six-Membered Rings and Related Chemistry. *J. Org. Chem.*, **1964**, *29*, 1543. (*c*) Campaigne, E. and Ellis, R.L. Substituted butyrolactones from ylidenemalononitriles. *ChemComm.*, **1966**, *5*, 140. (*d*) Campaigne, E. and Ellis, R.L., Cyclization of ylidenemalononitriles. V. Formation of substituted. gamma.-lactones. *J. Org. Chem.*, **1967**, *32*, 2372. (*e*)Wypych, J. C.; Nguyen, T. M.; Benechie, M.; Marazano, C. Reaction of aldimine anions with vinamidinium chloride: Three-component access to 3-alkylpyridines and 3-alkylpyridinium salts and access to 2-alkyl glutaconaldehyde derivatives. *J. Org. Chem*. **2008**, *73*, 1169.

18 (*a*) Schmidt, R. R. New synthesis of aryl substituted 3-azapyrylium salts and their reaction with CH-acidic compounds. *Chem. Ber*. **1965**, *98*, 3892. (*b*) Farhanullah, N.; Agarwal, N.; Goel, A.; Ram, V. J. J. Synthesis of Aminonicotinonitriles and Diaminopyridines through Base-Catalyzed Ring Transformation of 2 H-Pyran-2-ones. *J. Org. Chem.*, **2003**, *68*, 2983. (*c*) Villemin, D.; Belhadj, Z.; Cheikh, N.; Choukchou-Braham, N.; Bar, N.; Lohier, J.-F. Solventless convenient synthesis of new cyano-2-aminopyridine derivatives from enaminonitriles. *Tetrahedron Lett*., **2013**, *54*, 1664. (*d*) Ege, G.; Frey, H. O.; Schuck, Eine neue Synthese von 4-Dimethylamino-1, 3-butadien-1, 1-dicarbonitrilen und deren Cyclisierung zu 2-Amino-3-cyanopyridinen. *E. Synthesis*, **1979**.

19 de Souza, J.M.; Abdiaj, I.; Chen, J.; Hanson, K.; de Oliveira, K.T.; McQuade, D.T. Increasing Scope of Clickable Fluorophores: Electrophilic Substitution of Ylidenemalononitriles. *J. Org. Chem. Res*., **2020** ,*85*, 11822.

20 U.S.Patent 3,263,484.

21 de Souza, J.M.; Abdiaj, I.; Chen, J.; Hanson, K.; de Oliveira, K.T.; McQuade, D.T. Synthesis of multi-substituted pyridines from ylidenemalononitriles and their emission properties. *Org. Biomol. Chem.*, **2021**, *19*, 1991.

22 Kibou, Z.; Aissaoui, N.; Daoud, I.; Seijas, J.A.; Vázquez-Tato, M.P.; Klouche Khelil, N.; Choukchou-Braham, N. Efficient Synthesis of 2-Aminopyridine Derivatives: Antibacterial Activity Assessment and Molecular Docking Studies. *Molecules*, **2022**, *27*, 3439.

23 Rashid, M.A.; Ashraf, A.; Rehman, S.S.; Shahid, S.A.; Mahmood, A.; Faruq, M. 1, 4-diazepines: A review on synthesis, reactions and biological significance. *Curr. Org. Synth.*, **2019**, *16*, 709.

24 Muylaert, K.; Jatczak, M.; Mangelinckx, S.; V Stevens, C. Synthesis of pyrido-annelated diazepines, oxazepines and thiazepines. *Curr. Med. Chem.* **2016***, 23,* 4784*.*

LIST OF RESEARCH PUBLICATIONS

A. National/International Journals.

1. Published a paper entitled “Dimroth rearrangement to 2-*N*-alkylated amino pyridines: an unusual reaction of primary amines ylideneketonitriles” **Damodar Karuturi**, Mahesh Kalbagh, Prashantha Kamath, Mark Montgomery, Shrikant Abhiman Shete, Mukul Lal. *Synth. Commun.* **2022**, *52*, 433–444.

2. “Hydrogen Bond Assisted Reactivity of Ylideneketonitriles with 1° Amines: A Chemo Selective Synthesis of 2-Pyridone and 2-Aminopyridine Derivatives” **Damodar Karuturi**, Mahesh Kalbagh, Prashantha Kamath, Venunath Hapse, Alok Kumar Pandey, Mukul Lal. **Manuscript preparation is in progress**.

B. National/International Conference Proceedings.

1. Presented a poster entitled “Non-Covalent Interactions Directed Synthesis of Novel 2,3,5-trisubstituted Pyridine from Push-Pull Systems” **Damodar Karuturi**, Mahesh Kalbagh, Prashantha Kamath, Mark Montgomery, Shrikant Abhiman Shete, Mukul Lal. in the symposium ‘Sustainable chemistry and technology’ conducted by Syngenta Biosciences on 4th November 2019.

2. Presented a poster entitled “Hydrogen Bond Assisted Reactivity of Ylideneketonitriles with 1° Amines: A Chemo Selective Synthesis of 2-Pyridone and 2-Aminopyridine Derivatives” **Damodar Karuturi**, Mahesh Kalbagh, Prashantha Kamath, Venunath Hapse, Alok Kumar Pandey, Mukul Lal. at 12th India-Japan Science and Technology Conclave: International Conference on Frontier Areas of Science and Technology (ICFAST-2022) held at University of Hyderabad with **Poster No. CO-12**, during September 09-10, 2022.

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